WH 0 8 500

P26478.A03

Application No. 10/519,682

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Tetsuo NAGANO et al.

Group Art Unit: 1755

Appln. No : 10/519,682

(National Stage of PCT/JP2003/008585)

Examiner: Not Yet Assigned

I.A. Filed

July 7, 2003

For

: FLUORESCENT PROBE

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
U.S. Patent and Trademark Office
Customer Service Window, Mail Stop Amendment
Randolph Building
401 Dulany Street
Alexandria, VA 22314

Sir:

Further to the Information Disclosure Statement filed August 15, 2005, and in accordance with the duty of disclosure under 37 C.F.R. §§ 1.56, 1.97, and 1.98, Applicants hereby bring the following information to the attention of the Examiner, which includes information cited in a Supplementary European Search Report issued in connection with counterpart European Application No. EP 03 74 1232, mailed June 30, 2005. A copy of the Supplementary European Search Report is being submitted herewith. The Examiner is invited to review the Supplementary European Search Report to inspect the relevance indicated during European examination with respect to the documents cited therein.

(1) FP 0 314 480 A, and family member U.S. Patent No. 5,049,673;

(2) Rajendra Nath SEN et al., "The Condensation of Primary Alcohols with Resorcinol and Other Hydroxy Aromatic Compounds", J. Am. Chem. Soc., vol. 47, pp. 1079-1091 (1925), XP002332482;

- (3) WO 01/62755, and family members U.S. Patent Application PublicationNos. 2003/162298 A1 and 2005/064308 A1;
- (Nos. 2003/162298 A1 and 2005/064308 A1;
- (5) U.S. Patent No. 5,874,590;
- (6) JP 10 226688 A, and family member U.S. Patent No. 5,874,590; and
- (7) EP 1 069 21 A, and family member U.S. Patent No. \$6,525,088 B1.

Applicants also bring the to the attention of the Examiner the below documents which are cited in the specification of the above-identified application:

- (8) U.S. Patent No. 6,903,226;
- (9) U.S. Patent No. 6,403,623
- (10) R. KURDUKER et al., "Search for Physiologically Active Compounds", Proc. Indian. Acad. Sci. Sect. A., Vol. 57, pp. 280-287 (1963), which is cited on page 18 of the specification;
- (11) A. MINTA et al., "Fluorescent Indicators for Cytosolic Calcium Based on Rhodamine and Fluorescein Chromophores", J. Biol. Chem., Vol. 264, No. 14, pp. 8171-8178 (1989), which is cited on page 18 of the specification; and
- (12) P.K. Grover et al., "Xanthones. Part IV. A New Synthesis of Hydroxyxanthones and Hydroxybenzophenones," J. Chem. Sci. (London), pp. 3982-3985 (1955).

documents:

(13) U.S. Pat. App. Publication No. 2003/0157727;

- (14) U.S. Pat. App. Publication No. 2003/0153027;
- (15) U.S. Pat. App. Publication No. 2005/0037332;
- (%6) U.S. Pat. App. Publication No. 2005/0182253;
- (17) **\ U.S. Pat. App. Publication No. 2006/0030054**;
- (18) U.S. Application No. 10/531,664, which is a National Stage Application of PCT/JR2003/013179, and which published as WO 2004/040296;
- (19) U.S. Application No. 10/570,355, which is a National Stage Application of PCT/JP2004/013185, and which published as WØ 2005/024049;
- (20) U.S. Pat. App. No. 11/433,691, which is a coptinuation of 10/994,380 which published as U.S. Pat. App. Publication No. 2005/0064308, which is a divisional of 10/203,628, and now U.S. Pat. No. 6,903,226;
- (21) U.S. Pat. App. No. 11/382,424 which is a continuation of U.S. Application No. 10/204,417 which published as U.S. Pat. App. Publication No. 2003/0153027, and which U.S. Application No. 10/204,417 is a National Stage Application of PCT/JP2001/01504, and which published as WO 01/63265;
- (22) U.S. Pat. No 6,756,231;
- (23) U.S. Pat. No. 6,469,051;
- (24) U.S. Fat. No. 6,441,197;
- (25) U.S. Pat. App. Publication No. 2005/0123478;
- (26) U.S. Pat. App. Publication No. 2005/0130314;
- (27) U.S. Pat. App. Publication No. 2004/0147035;
- (28) U.S. Pat. App. Publication No. 2004/0043498;
- (29) U.S. Patent No. 6,013,802;

- (30) U.S. Patent No. 6,833,386;
- (31) U.S. Patent No. 6,569,892;
- 🚱2) U.S. Patent No. 5,874,590;
- (33) U.S. Patent No. 5,648,270;
- (34) U.S. Patent No. 6,441,197;
- (35) U.S. Patent No. 6,469,051;
- (36) U.S. Pate No. 6,525,088;
- (37) U.S. Patent No. 6,569,892;
- (38) U.S. Patent No. 6,201,134;
- (39) U.S. Patent No. 5,208 148;
- (40) Reyes, J.G., et al., Biol. Res., 27, pp 49-56, 1994;
- (41) Tsuda, M., et al., Neurosci., 17, pp. 6678-6684, 1997;
- (42) Koike, T., et al., J. Am. Chem. Soc., 118, pp. 12696-12703, 1996;
- (43) Saibou Kougaku (Cell Technology), 17, pp. 584-595, 1998;
- (44) Tanpakushitsu.Kakusan.Kouso (Protein, Nucleic Acid and Enzyme), extra number, 42, pp. 1/1-176, 1997;
- (45) Tetsuji Kametani, Nankodo Co., Ltd., pp. 214-215, 1997;
- (46) Handbook of Fluorescent Probes and Research Chemicals, 6th Edition by Richard P. Haugland, pp. 503 and 531-540;
- (47) Protective Groups in Organic Synthesis, T. W. Greene, John Wiley & Sons, Inc. pp. v-xxi and 369-405;
- JP 2000-239272 A (T. NAGANO et al.), 5 September 2000, accompanied by an English language abstract thereof (provided by Patent Abstracts of Japan);

- (49) Angew. Chem., Int. Ed. (1999), 38(21), pp. 3209-3212;
- (50) Anal. Chem. (1998), 70(13), pp. 2446-2453;
- (\$1) Bioorganic & Medicinal Chemistry, Vol.4, No.6, pp. 901-916, (1996);
- (52) Bioorg. Khim. (1995), 21(10), pp. 795-801;
- (53) Soi, China, Ser. B: Chem. (1998), 41(5), pp. 549-555;
- (54) J. Am. Chem. Soc. (1996), 118, pp. 6514-6515;
- (55) Hirano T. et al., "Highly Zinc-Selective Fluorescent Sensor Molecules Suitable for Biological Applications", J. Am. Chem. Soc., Vol. 122, No. 49, 13 December 2003, pp. 12399-12400;
- (56) Walkup G. K. et al., "New Cell-Permeable Fluorescent Probe for Zn²⁺", J. Am. Chem. Soc., Vol. 122, No. 23, 14 June 2000, pp. 5644-5645;
- (57) WO 00/00819;
- (58) WO 89/09408;
- (59) WO 96/42016;
- (60) WO 98/15830;
- (61) WO 99/15896;
- (62) BAMBOT, S.F. et al., "Potential Applications of lifetime-Based, Phase-Modulation Fluorimetry in Bioprocess and Clinical Monitoring", Trends in Biotechnology, Vol. 13, No. 3, March 1995, pages 106-115, XP 004207135;
- (63) SIPIOR, J. et al., "Lifetime-Based Optical Sensing of pH Using Resonance Energy Transfer in Sol-Gel Films", Sensors and Actuators B; Vol. 22, No. 3, December 1994, pages 181-188, XP004011062;

- (64) SELVIN, P.R. et al., "Luminescence Energy Transfer Using a Terbium Chelate: Improvements on Fluorescence Energy Transfer", Proceedings of the National Academy of Science of USA, National Academy of Science, Washington, DC, US, Vol. 91, October 1994, Pages 10024-10028;
- (65) U.S. Ratent No. 5,656,433, and family members U.S. Patent Nos. 5.622,821, and 5,639,615;
- (66) Yuan, J. et al. "Functionalization of Fluorescent Lanthanide Complexes and Their Applications to Biotechnology", Bunseki Kagaku Japan Analyst; Vol. 48, No. 12, pages 1077-1087 (1999), XP002932633;
- (67) JP 9-101262 A (GOLIGHT INC), 16 April 1997, accompanied by an English language abstract thereof.
- (68) U.S. Patent No. 4,891,075;
- (69) U.S. Patent No. 4,968,63/
- (70) U.S. Patent No. 5,340,716;
- (71) U.S. Patent No. 5/800,996;
- (72) U.S. Patent No. 5,863,727;
- (73) JP 5-180 (73) A, accompanied by an English language abstract thereof;
- (74) JP 10/88124 A, accompanied by an English language abstract thereof;
- (75) JP 2000-111480 A, accompanied by an English language abstract thereof;
- (16) Rogers, M. V., Drug Discovery Today, Vol. 2, pp. 156-160, 1997;
- (77) Selvin, P. R., et al., J. Am. Chem. Soc., Vol. 117, pp. 8132-8138, 1995;
- (78) Stryer, L., Ann. Rev. Biochem., Vol. 47, pp. 819-846, 1978;

- (79) Hemmilä, I., et al., Drug Discovery Today, Vol. 2, pp. 373-381, 1997;
- (80) New Apoptosis Experimental Protocol, 2nd ed., Yodosha, pp. 201-204, 1999;
- (81) Selvin, P. R., et al., J. Am. Chem. Soc., Vol. 116, pp. 6029-6030, 1994;
- (82) J. BURCH, "The Inhibition of Horse-Liver Esterase by Rhodamine B," Biochemical Journal, Vol. 59, pp. 97-110 (1955);
- (83) D.D. THOMAS et al., "Flourescence energy transfer in the rapid-diffusion limit," Proceedings of the National Academy of Sciences of the United States of America, Vol. 75, No. 12, pp. 5746-5750 (1978);
- (84) S.M. YEH et al., "Characterization of Transferin Metal-Binding Sites by Diffusion-Enhanced Energy Transfer, Biochemistry, 19, pp. 5057-5062 (1980);
- (85) R.A. EDWARDS et al., "Spectroscopic Studies of Cibacron Blue and Congo Red Bound to Delydrogenases and Kinases. Evaluation of Dyes as Probes of the Dipucleotide Fold," Biochemistry, Vol. 18, No. 23, pp. 5197-5204 (1979).
- (86) C.F. MEARES et al., "Diffusion-Enhanced Energy Transfer Shows Accessibility of Ribonucleic Acid Polymerase Inhibitor Binding Sites," Biochemistry, 20, pp. 610-617 (1981);
- (87) T.S. WENSEL et al., "Electrostatic Properties of Myoglobin Probed by Diffusion-Enhanced Energy Transfer," Biochemistry, 22, pp. 6217-6254 (1983);

- (88) M.M. FEDERICI et al., "Interaction of Cibacron Blue F₃GA with Glutamine Synthetase: Use of the Dye as a Conformational Probe. 1. Studies Using Unfractionated Dye Samples," Biochemistry, 24, pp. 647-660 (1985);
- (89) T.G. WENSEL et al., "Diffusion-Enhanced Lanthanide Energy Transfer Study of DNA-Bound Cobalt(III) Bleomycins: Comparisons of Accessibility and Electrostatic Potential with DNA Complexes of Ethidium and Acridine Orange," Biochemistry, 24, pp. 3060-3069 (1985);
- (90) B.S. ISAACS at al., "A Domain of Membrane-Bound Coagulation Factor
 Va Is Located Far from the Phospholipid Surface. A Fluorescence Energy
 Transfer Measurement," Biochemistry, 25, pp. 4958-5969 (1986);
- (91) T.G. WENSEL et al., "Study of Biological Macromolecules by Diffusion-Enhanced Lanthanide Energy Transfer," Journal of the Less-Common Metals, 149, pp. 143-160 (1989);
- (92) P.R. SELVIN et al., "Luminescence Resonance Energy Transfer," Journal of the American Chemical Society, 116, pp. 6029-6030 (1994);
- (93) T. YAMAMOTO of al., "Determination of Electrostatic Potential Around Specific Locations on the Surface of Actin by Diffusion-enhanced Fluorescence Resonance Energy Transfer," Journal of Molecular Biology, 241, pp. 714-731 (1994);
- (94) S.C.J. MESKERS et al., "Analysis of Delayed Luminescence from Some Quenchers of Tb(DPA)₃³- Emission: Proof for an Energy Transfer Quenching Mechanism," Journal of Alloys and Compounds, 250, pp. 332-335 (1997);

- (95) D.D. ROOT, "In situ Molecular Association of Dystrophin with Actin Revealed by Sensitized Emission Immuno-Resonance Energy Transfer"

 Proceedings of the National Academy of Sciences of the United States of America, 94, pp. 5685-5690 (1997);
- (96) C. MUCIGNAT-CARETTA et al., "Building of Two Fluorescent cAMP Analogues to Type I and II Regulatory Subunits of cAMP-Dependent Protein Kinases," Biochimica et Biophysica Acta, 1357, pp. 81-90 (1997);
- (97) Y.-W. PARK et al., "Homogeneous Proximity Tyrosine Kinase Assays:

 Scintillation Proximity Assay versus Homogeneous Time-resolved

 Fluorescence," Analytical Biochemistry, 269, pp. 94-104 (1999);
- (98) K. BLOMBERG et al., "Terbium and Rhodamine as Labels in a Homogeneous Time-resolved Fluorometric Energy Transfer Assay of the β Subunit of Human Chorionic Gonadotropin in Serum," Clinical Chemistry, 45, 855-861 (1999);
- (99) L.L. PEARCE et al., "Role of Metallothionein in Nitric Oxide Signaling as Revealed by a Green Fluorescent Fusion Protein," Proceedings of the National Academy of Sciences of the United States of America, 97, pp. 477-482 (2000);
- (100) M. KØRESAWA et al., "Development of a Time-Resolved Fluorometric Detection System Using Diffusion-Enhanced Energy Transfer," Analytical Chemistry, 72, pp. 4904-4907 (2000);
- (101) U.S. Patent No. 5,037,615;
- (102) U.S. Patent No. 5,246,867;
- (103) U.S. Patent No. 5,622,821;

- (104) U.S. Patent No. 6,753,156;
- (105) U.S. Patent No. 6,936,687;
- (**1**06) U.S. Patent No. 6,972,182;
- (107) U.S. Patent Application Publication No. 2002/0177120;
- (108) U.S. Patent No. 5,623,080;
- (109) U.S. Patent No. 6,525,088;
- (110) EP 0515133 A2;
- (111) JP 60-54381 A accompanied by an English language abstract thereof;
- (112) T. NAGANO et al., "Specific Detection Method and Useful Generating System of Singlet Oxygen," Free Radicals in Clinical Medicine, Vol. 7, pp. 35-41 (1993);
- (113) I. SAITO et al., "Methyl-Substituted Poly(vinylnaphthalene) as a Reversible Singlet Oxygen Carrier," J. Am. Chem. Soc., Vol. 107, pp. 6329-6334, 1985;
- (114) T. W. Greene et al., "rotective Groups in Organic Synthesis," John Wiley & Sons, Inc., pp. y-xxi and 369-405 (1981);
- (115) J. KABATC et al., "Free Radical Polymerization Initiated via Photoinduced Intermolecular Electron Transfer Process: Kinetic Study 3¹," Polymer 40(3) pp. 735-745 (1999);
- (116) K SETSUKINAI et al., "Fluorescence Switching by O-dearylation of 7-aryloxycoumarins. Development of Novel Flourescence Probes to Detect Reactive Oxygen," J. Chem. Soc., Perkin Trans. 2, 12, pp. 2453-2457, (2000);
- (117) U.S. Patent No. 6,903,226;

- (118) J.W. FIRTH et al., "Some Phenoxy-2H-benzo[b]pyrans," J. Chem. Research (S), Vol. 2000, No. 7, pp. 308-308 (July 2000).
- (**1**9) U.S. Patent No. 6,656,927;
- (120) J.G. REYES et al., "A Fluorescence Method to Determine Picomole

 Amounts of Zn(II) in Biological Systems," Biol. Res., Vol. 27, pp. 49-56,

 (1994)
- (121) M. TSUDA et al., "Expression of Zinc Transporter Gene, ZnT-1, Is

 Induced After Transient Forebrain Ischemia in the Gerbil," The Journal of

 Neuroscience, Vol. 17, No. 17, pp. 6678-6684 (September 1, 1997);
- (122) T. KOIKE et al., "A Novel Biomimetic Zinc(II) Fluorophore,

 Dansylamidoethyl-Pendan Macrocyclic Tetraamine 1,4,7,10
 Tetraazacyclododecane (Cyclen) "J. Am. Chem. Soc., Vol. 118, 1996, pp. 12696-12703;
- (123) WO 01/62755, together with patent family member U.S. Patent Application Publication No. 2003/162298 A1;
- (124) Japanese Laid-Open Patent Publication No. 2000-239272, together with an English lappuage Abstract of the same;
- (125) Web site of the Pharmaceutical Society of Japan, on Pebruary 1, 2003, a copy of the screenshot is enclosed. The subject matter of the screenshot was then published in an Abstract of "The 123rd Annual Congress of the Pharmaceutical Society of Japan" on March 5, 2003 for presentation No. 29[P1]I-219 entitled "Development of Fluorescent Probe Having Low Affinity for Zinc" in the 123rd Annual Congress of the Pharmaceutical Society of Japan held on March 27-29, 2003;

- (126) Newport Green: A Catalog of Molecular Probes, Inc. "Handbook of Fluorescent Probes and Research Chemical, Chapter 22 Section 22.7 Fluorescent Indicators for Zn²⁺ and Other Metals", 6th Edition by Richard P. Haugland, pp. 531-540 (1996);
- (127) Tochiaki HIRATSUKA, "Tanpakushitsu-Kakusan-Kouso (Protein, Nucleic Acid and Enzyme)", Vol. 42, No. 7, pp. 171-176 (1997);
- (128) ANDEREGG et al., Helvetica Chimica Acta, Vo.. 50, pp. 2330-2333 (1967);
- (129) T. HIRANO et al., "Highly Zinc-Selective Fluorescent Sensor Molecules Suitable for Biological Applications," Journal of the American Chemical Society, Vol. 122, No. 49, pp. 12399-12400 (2000);
- (130) R.P. HAUGLAND, "Handbook of Fluorescent probes and Research Products," 9th Edition Supplement, Chapter 20, pp. 805-817 (2002);
- (131) G.K. WALKUP et al., "A New Cell-Permeable Fluorescent Probe for Zn²⁺,"

 Journal of the American Chemical Society, Vol. 122, No. 23, pp. 5644
 5645 (2000);
- (132) J. KAWAKAM et al., "Ab initio Molecular Orbital Study of Emission

 Mechanism of 2,6-Bis (quinolinecarboxy) methylpyridine as Fluorescent

 Chemosensors for Zinc and Cadmium Ions," Journal of Computer

 Chemistry, Japan, Vol. 2, No. 2, pp. 57-62 (2003);
- (133) C.J. FREDERICKSON et al., "A quinoline fluorescence method for visualizing and assaying the histochemically reactive zinc (bouton zinc) in the brain," Journal of Neuroscience Methods, Vol. 20, pp 91-103 (1987);

- (134) D. ZALEWSKI et al., "Correlation of apoptosis with change in intracellular labile Zn(II) using Zinquin [(2-methyl-8-*p*-toluenesulphonamido-6-quinolyloxy)acetic acid], a new specific fluorescent probe for Zn(II),"

 Biochemical Journal, Vol. 296, Part 2, pp. 403-408 (1993);
- (135) WQ 01/64664 A1, accompanied by family member EP 1 260/508 A1;
- (136) JP 06 211831, accompanied by an English language abstract and family member U.S. Patent No. 5,451,343;
- (137) William A. PR OR et al., "A Practical Method for Preparing Peroxynitrite Solutions of Low Ionic Strength and Free of Hydrogen Peroxide," Free Radical Biology & Medicine", Vol. 18, No. 1, pp. 75-83 (1995);
- (138) Stephen L. HEMPEL et al., "Dihydrofluorescein Diacetate is Superior for Detecting Intracellular Oxidants: Comparison with 2',7'-Dichlorodihydrofluorescein Diacetate, 5(and 6)-Carboxy-2',7'-Dichlorodihydrofluorescein Diacetate, and Dihydrorhodamie 123," Free Radical Biology & Medicine, Vol. 27, Nos. 1/2, pp. 146-159 (1999); and
- (139) Joseph A. HRABLE et al., "New Nitric Oxide-Releasing Zwitterions Derived from Polyamires," J. Org. Chem. Vol. 58, pp. 1472-1476 (1993).

Further to the U.S. Patent and Trademark Office's decision to waive the requirement under 77 C.F.R 1.98, copies of the U.S. patents and U.S. published patent applications are not enclosed herewith. However, if any copies are reeded, the Examiner is respectfully requested to contact the undersigned.

published patent applications, are enclosed together with a duly completed Form PTO The Examiner is accordingly requested to consider each of these documents,

and to make them of record in this application by initialing in the appropriate spaces on the Form-1449. Applicants respectfully request that the Examiner include a copy of the initialed Form PTO-1449 with the next communication from the U.S. Patent and Trademark Office.

Applicants note that while this Supplemental Information Disclosure Statement is being filed more than three months from the filing date, Applicants have not received an action on the merits from the U.S. Patent and Trademark Office. Accordingly, consideration of the enclosed document is required under 37 O.F.R. 1.97(b)(3).

However, if an action on the merits has been mailed prior to the filing date of this Supplemental Information Disclosure Statement, Applicants hereby authorize the charging of any required fees necessary for consideration of the documents cited herein to Deposit Account No. 19-0089.

Any comments or questions concerning this application can be directed to the undersigned at the telephone number given below.

Respectfully submitted, Tetsuo NAGANO et al.

Bruce H. Bernstein

Reg. No. 29,027 Stephen M. Roylance Reg. No. 31,296

June 2, 2006
GREENBLUM & BERNSTEIN, P.L.C.
1950 Roland Clarke Place
Reston, VA 20191
(703) 716-1191

FORM PTO-1449

0.5. Department of Commerce Patent and Trademark Office

Atty. Docket No. P26478

Application 10/519,682

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary) Applicant Tetsuo NAGANO et al.

Filing Date I.A. Filed July 7, 2003 Ground 1755

EXAMINER	T								0.0. I AIL	IT DOCUMENTS		<u> </u>	FILING DATE
INITIAL			DOG	CUME	ENT	NUM	BER		DATE	NAME	CLASS	SUBCLASS	IF APPROPRIATE
-		5	0	4	9	6	7	3	09/17/91	TSIEN et al.			
	2003 /	0	1	6	2	2	9	8	08/28/03	NAGANO et al.			
	2005 /	0	0	6	4	3	0	8	03/24/05	NAGANO et al.			
		5	8	7	4	5	9	0	02/23/99	NAGANO et al.			
		6	5	2	5	0	8	8	02/25/03	NAGANO et al.			
		6	9	0	3	2	2	6	06/07/05	NAGANO et al.			
		6	4	0	3	6	2	5	06/11/02	NAGANO et al.			
	2003 /	0	1	5	7	7	2	7	08/21/03	NAGANO et al.			
	2003 /	0	1	5	3	0	2	7	08/14/03	NAGANO et al.			
	2005 /	0	0	3	7	3	3	2	02/17/05	KOMATSU et al.,			
	2005 /	0	1	8	2	2	5	3	08/18/05	YANO et al.			
	2006 /	0	0	3	0	0	5	4	02/09/06	NAGANO et al.			
	2003 /	0	1	5	3	0	2	7	08/14/03	NAGANO et al.			
		6	7	5	6	2	3	1	06/29/04	NAGANO et al.			
		6	4	6	9	0	5	1	10/22/02	NAGANO et al.			
		6	4	4	1	1	9	7	08/27/02	NAGANO et al.			
	2005 /	0	1	2	3	4	7	8	06/09/05	NAGANO et al.			
	2005 /	0	1	3	0	3	1	4	06/16/05	NAGANO et al.		, , , , , , , , , , , , , , , , , , , ,	
	2004 /	0	1	4	7	0	3	5	07/29/04	NAGANO et al.			
	2004 /	0	0	4	3	4	9	8	03/04/04	NAGANO et al.			
		6	0	1	3	8	0	2	01/11/00	HOYLAND et al.			
		6	8	3	3	3	8	6	12/21/04	NAGANO et al.			
		6	5	6	9	8	9	2	05/27/03	NAGANO et al.			
		5	6	4	8	2	7	0	07/15/97	KUHN et al.			
		6	5	6	9	8	9	2	05/27/03	NAGANO et al.			
		6	2	0	1	1	3	4	03/13/01	NAGANO et al.			
-		5	2	0	8	1	4	8	05/04/93	HAUGLAND et al.			
		5	6	5	6	4	3	3	08/12/97	SELVIN et al.			
		5	6	2	2	8	2	1	04/22/97	SELVIN et al.			
		5	6	3	9	6	1	5	06/17/97	SELVIN et al.			
		4	8	9	1	0	7	5	01/02/90	DAKUBU et al.			

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449

		100100c W
U.S. Department of Commerce Patent and Trademark Office		Application No. 10/519,682
SURE STATEMENT	Applicant	<u> </u>

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)

Tetsuo NAGANO et al.

Filing Date I.A. Filed July 7, 2003

Group 1755

U.S. PATENT DOCUMENTS

EXAMINER INITIAL			DOG	CUME	ENT	NUM	BER		DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
		4	9	6	8	6	3	1	11/06/90	DAKUBU			
		5	3	4	0	7	1	6	08/23/94	UIIMAN et al.			
		5	8	0	0	9	9	6	09/01/98	LEE et al.			
		5	8	6	3	7	2	7	01/26/99	LEE et al.			
		5	0	3	7	6	1	5	08/06/91	KANE			
		5	2	4	6	8	6	7	09/21/93	LAKOWIEZ et al.			
		5	6	2	2	8	2	1	04/22/97	SELVIN et al.			
		6	7	5	3	1	5	6	06/22/04	MATHIS et al.			
		6	9	3	6	6	8	7	08/30/05	KOMORIYA et al.			
		6	9	7	2	1	8	2	12/06/05	COLYER et al.			
	2002 /	0	1	7	7	1	2	0	11/28/02	ELLIOTT et al.,			
_		5	6	2	3	0	8	0	04/22/97	NECKERS et al.			
		6	5	2	5	0	8	8	02/25/03	NAGANO et al.			
		6	6	5	6	9	2	7	12/02/03	NAGANO et al.			

FOREIGN PATENT DOCUMENTS

E														TRANS	
			DO	CUME	ENT	NUM	BER		DATE	<u>'</u>	COUNTRY	CLASS	SUBCLASS	YES	NO
		0	3	1	4	4	8	0	05/03/89	EPC)		_		
	0	1	1	6	2	7	5	5	08/30/01	WIP	0				
		1	2	6	0	5	1	0	11/27/02	EPC)				
	10	-	2	2	6	6	8	8	08/25/98	JAP.	AN				
		1	0	6	9	1	2	1	01/17/01	EPC)				
	2004	1	0	4	0	2	9	6	05/13/04	WIP	0				_
	2005	1	0	2	4	0	4	9	03/17/05	WIP	0				
	0	1	1	6	3	2	6	5	08/30/01	WIP	0				
	2000	-	2	3	9	2	7	2	05/09/00	JAP.	AN				
	0	0	1	0	0	8	1	9	01/06/00	WIP	0				
	8	9	1	0	9	4	0	8	10/05/89	WIP	0				
	9	6	1	4	2	0	1	6	12/27/96	WIP	0				
	9	8	1	1	5	8	3	0	04/16/98	WIP	0				
	9	9	1	1	5	8	9	6	04/01/99	WIP	0				
EXAMINER	. /	Tao	fiq S	Soloi	a/			-			DATE CONS	SIDERED	03/31/2008		

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office												
		IATION DISCLOSURE STA BY APPLICANT			Applican Tetsuo N	t NAGANO et	al.					
(Use several sheets if necessary)						Filing Date Group I.A. Filed July 7, 2003 1755						
			FOREIGN PAT	ENT DOCU	MENTS							
								TRANSLATION				

									FOREIGN PAT	ENT DOC	JMENTS					
			DOC	CUMI	ENT	NUM	BER		DATE	CO	JNTRY	CLASS	SUBC	LASS	TRAN: YES	SLATION
	9	-	1	0	1	2	6	2	04/15/97	JAPAN						
	5	-	1	8	0	7	7	3	07/23/99	JAPAN						
	10	-	0	8	8	1	2	4	04/07/98	JAPAN						
	2000	-	1	1	1	4 8 0 04/21/00 JAPAN										
		0	5	1	5	1	3	3	11/25/92	EPO						
	60	-	0	5	4	3	8	1	03/28/85	JAPAN	<u> </u>					
	0	1	1	6	4	6	6	4	09/07/01	WIPO						
		1	2	6	0	5	0	8	11/27/02	EPO						
	6	-	2	1	1	8	3	1	08/02/94	JAPAN						
														-		
		•		0.	THEF	R DO	CUM	ENT	S (Including A	uthor, Title	, Date, Pert	inent Pages, E	tc.)			<u> </u>
	1	En	glis	h La	ngu	age	Abs	trac	t of JP 2000	-239272						
	2	En	glis	h La	ngu	age	Abs	trac	t of JP 9-10	1262.						
	3	En	glis	h La	ngu	age	Abs	trac	t of JP 5-18	0773.	_			_		
	4	En	glis	h La	ngu	age	Abs	trac	t of JP 10-8	8124.	_					
	5	En	glis	h La	ngu	age	Abs	trac	t of JP 2000	-111480						
	6	En	glis	h La	ıngu	age	Abs	trac	t of JP 60-0	54381.						
	7	En	glis	h La	ngu	age	Abs	trac	t of JP 6-21	1831.						
	8	Ra	jeno	dra I	Nath	SE	N et	al.,	"The Conde	ensation o	of Primary	Alcohols wit	h Resor	cinol ar	nd Other	
		Ну	dro	ху А	rom	atic	Con	npoi	unds", J. Am	. Chem.	Soc., vol.	47, pp. 1079	-1091 (1925), >	(P00233	2482.
	9	R.	KU	RDU	JKE	R et	al.,	"Se	arch for Phy	siologica	lly Active (Compounds"	, Proc. I	ndian. A	Acad. Sc	i.
		Se	ct. A	4., V	ol. s	57, p	p. 2	80-2	287 (1963).							
	10	A.	MIN	ATA	et a	l., "F	luor	esc	ent Indicator	s for Cyt	osolic Cal	cium Based	on Rhoo	damine	and	
		Flu	ore	scei	n Cl	hron	nopt	nore	s", J. Biol. C	hem., Vo	I. 264, No	. 14, pp. 817	'1-8178	(1989).		
	11	P.I	K. G	rove	er et	al.,	"Xa	ntho	nes. Part IV	. A New	Synthesis	of Hydroxyx	anthone	s and		
		Ну	dro	xybe	enzo	phe	non	es,"	J. Chem. So	ci. (Londo	on), pp. 39	82-3985 (19	55).			
XAMINER	·	/	Tac	ofiq (Solo	ıla/				DA	TE CON	SIDERED	03	/31/200	8	

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

U.S. Department of Commerce	

FORM PTO-1449	U.S. Department of Commerce Patent and Trademark Office		Application No. 10/519,682
INFO	RMATION DISCLOSURE STATEMENT BY APPLICANT	Applicant Tetsuo NAGANO et al.	
	(Use several sheets if necessary)	Filing Date I.A. Filed July 7, 2003	Group 1755
	OTHER DOCUMENTS (Including Author, Title	e, Date, Pertinent Pages, Etc.)	
1	Reyes, J.G., et al., Biol. Res., 27, pp. 49-56, 19	94.	
1	Tsuda, M., et al., Neurosci., 17, pp. 6678-6684	1997.	-
1	Koike, T., et al., J. Am. Chem. Soc., 118, pp. 1	2696-12703, 1996.	
1	Saibou Kougaku (Cell Technology), 17, pp. 584	1-595, 1998.	
1	Tanpakushitsu.Kakusan.Kouso (Protein, Nucle	ic Acid and Enzyme), extra	number, 42, pp. 171-176,
	1997.		
1	Tetsuji Kametani, Nankodo Co., Ltd., pp. 214-2	15, 1997.	
1	Handbook of Fluorescent Probes and Researc	n Chemicals, 6th Edition by	Richard P. Haugland,
	pp. 503 and 531-540.		
1	Protective Groups in Organic Synthesis, T. W.	Greene, John Wiley & Sons	s, Inc. pp. v-xxi and 369-
	405.		
2	Angew. Chem., Int. Ed. (1999), 38(21), pp. 320	9-3212	
2	Anal. Chem. (1998), 70(13), pp. 2446-2453		
2	Bioorganic & Medicinal Chemistry, Vol.4, No.6,	pp. 901-916, (1996)	
2	Bioorg. Khim. (1995), 21(10), pp. 795-801		
2	Sci. China, Ser. B: Chem. (1998), 41(5), pp. 54	9-555	
2	J. Am. Chem. Soc. (1996), 118, pp. 6514-6515		
2	Hirano T. et al., "Highly Zinc-Selective Fluoresc	ent Sensor Molecules Suita	able for Biological
	Applications", J. Am. Chem. Soc., Vol. 122, No	. 49, 13 December 2000, pp	p. 12399-12400.
2	Walkup G. K. et al., "A New Cell-Permeable Flu	iorescent Probe for Zn ²⁺ ", J	l. Am. Chem. Soc., Vol.
	122, No. 23, 14 June 2000, pp. 5644-5645.		
2	BAMBOT, S.B. et al., "Potential Applications of	Lifetime-Based, Phase-Mo	dulation Fluorimetry in
	Bioprocess and Clinical Monitoring", Trends in	Biotechnology, Vol. 13, No.	3, March 1995, pages
	106-115, XP 004207135.		
2	SIPIOR, J. et al., "Lifetime-Based Optical Sens	ing of pH Using Resonance	Energy Transfer in Sol-
	Gel Films", Sensors and Actuators B; Vol. 22, I	No. 3, December 1994, pag	es 181-188,
	XP004011062.		
3	SELVIN, P.R. et al., "Luminescence Energy Tra	ansfer Using a Terbium Che	elate: Improvements on
	Fluorescence Energy Transfer", Proceedings of	f the National Academy of S	Science of USA, National
	Academy of Science, Washington, DC, US, Vo	l. 91, October 1994, Pages	10024-10028.
3	Yuan, J. et al., "Functionalization of Fluorescer	t Lanthanide Complexes ar	nd Their Applications to
	Biotechnology", Bunseki Kagaku – Japan Anal	yst; Vol. 48, No. 12, pages	1077-1083 (1999),
	XP002932633.		
EXAMINER	/Taofiq Solola/	ATE CONSIDERED	03/31/2008

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-14	449	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. P26478	Application No. 10/519,682
IN	FORM	ATION DISCLOSURE STATEMENT BY APPLICANT	Applicant Tetsuo NAGANO et al.	
	(Us	se several sheets if necessary)	Filing Date I.A. Filed July 7, 2003	Group 1755
		OTHER DOCUMENTS (Including Author, Title,	Date, Pertinent Pages, Etc.)	
	32	Rogers, M. V., Drug Discovery Today, Vol. 2, pp	. 156-160, 1997.	
	33	Selvin, P. R., et al., J. Am. Chem. Soc., Vol. 117	, pp. 8132-8138, 1995.	
	34	Stryer, L., Ann. Rev. Biochem., Vol. 47, pp. 819-	846, 1978.	
	35	Hemmilä, I., et al., Drug Discovery Today, Vol. 2	, pp. 373-381, 1997.	
	36	New Apoptosis Experimental Protocol, 2nd ed.,	Yodosha, pp. 201-204, 199	9.
	37	Selvin, P. R., et al., J. Am. Chem. Soc., Vol. 116	, pp. 6029-6030, 1994.	· · · · · · · · · · · · · · · · · · ·
	38	J. BURCH, "The Inhibition of Horse-Liver Estera	se by Rhodamine B," Bioch	emical Journal, Vol. 59,
		pp. 97-110 (1955).		
	39	D.D. THOMAS et al., "Flourescence energy tran	sfer in the rapid-diffusion lin	nit," Proceedings of the
- 1		National Academy of Sciences of the United Sta	tes of America, Vol. 75, No.	12, pp. 5746-5750
		(1978).		
	40	S.M. YEH et al., "Characterization of Transferin	Metal-Binding Sites by Diffu	sion-Enhanced Energy
		Transfer," Biochemistry, 19, pp. 5057-5062 (198		
	41	R.A. EDWARDS et al., "Spectroscopic Studies of	of Cibacron Blue and Congo	Red Bound to
		Dehydrogenases and Kinases. Evaluation of Dy	es as Probes of the Dinucle	eotide Fold,"
		Biochemistry, Vol. 18, No. 23, pp. 5197-5204 (1	979).	
	42	C.F. MEARES et al., "Diffusion-Enhanced Energ	y Transfer Shows Accessib	ility of Ribonucleic Acid
		Polymerase Inhibitor Binding Sites," Biochemisti	y, 20, pp. 610-617 (1981).	
	43	T.G. WENSEL et al., "Electrostatic Properties of	Myoglobin Probed by Diffus	sion-Enhanced Energy
		Transfer," Biochemistry, 22, pp. 6247-6254 (198	3).	
	44	M.M. FEDERICI et al., "Interaction of Cibacron E	Blue F ₃ GA with Glutamine S	ynthetase: Use of the
		Dye as a Conformational Probe. 1. Studies Usin		
		pp. 647-660 (1985).		
	45	T.G. WENSEL et al., "Diffusion-Enhanced Lanth	anide Energy-Transfer Stud	ly of DNA-Bound
		Cobalt(III) Bleomycins: Comparisons of Accessi	bility and Electrostatic Poter	ntial with DNA
		Complexes of Ethidium and Acridine Orange," B	iochemistry, 24, pp. 3060-3	069 (1985)
	46	B.S. ISAACS et al., "A Domain of Membrane-Bo		
		Phospholipid Surface. A Fluorescence Energy T	ransfer Measurement," Biod	chemistry, 25, pp. 4958-
		5969 (1986).		
	47	T.G. WENSEL et al., "Study of Biological Macro	molecules by Diffusion-Enha	anced Lanthanide
		Energy Transfer," Journal of the Less-Common Metal		
	48	P.R. SELVIN et al., "Luminescence Resonance Energ	gy Transfer," Journal of the Am	erican Chemical Society,
		116, pp. 6029-6030 (1994).		
EXAMINER 7	aofiq	Solola/ DA	TE CONSIDERED 03/	/31/2008

EXAMINER Tracing Soloia/ DATE CONSIDERED 03/31/2008

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

EXAMINER

P26478.P10				UD 19002 - CIAUSheeDSA
FORM PTO-1	449	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. P26478	Application No. 10/519,682
IN	FORMA	ATION DISCLOSURE STATEMENT BY APPLICANT	Applicant Tetsuo NAGANO et al.	
	(Us	e several sheets if necessary)	Filing Date I.A. Filed July 7, 2003	Group 1755
		OTHER DOCUMENTS (Including Author, Title,	Date, Pertinent Pages, Etc.)	
	49	T. YAMAMOTO et al., "Determination of Electro	static Potential Around Spe	ecific Locations on the
		Surface of Actin by Diffusion-enhanced Fluores	cence Resonance Energy	Transfer," Journal of
		Molecular Biology, 241, pp. 714-731 (1994).		
	50	S.C.J. MESKERS et al., "Analysis of Delayed Lu	uminescence from Some Q	uenchers of Tb(DPA) ₃ ³ -
		Emission: Proof for an Energy Transfer Quench	ing Mechanism," Journal o	f Alloys and Compounds,
		250, pp. 332-335 (1997).		
	51	D.D. ROOT, "In situ Molecular Association of Dy	strophin with Actin Reveal	ed by Sensitized
		Emission Immuno-Resonance Energy Transfer,	" Proceedings of the Nation	nal Academy of Sciences
		of the United States of America, 94, pp. 5685-56	690 (1997).	
	52	C. MUCIGNAT-CARETTA et al., "Building of Tw	o Fluorescent cAMP Analo	ogues to Type I and II
		Regulatory Subunits of cAMP-Dependent Prote	in Kinases," Biochimica et l	Biophysica Acta, 1357,
		pp. 81-90 (1997).		
	53	YW. PARK et al., "Homogeneous Proximity Ty	rosine Kinase Assays: Scir	ntillation Proximity Assay
		versus Homogeneous Time-resolved Fluoresce	nce," Analytical Biochemist	try, 269, pp. 94-104
		(1999).		
	54	K. BLOMBERG et al., "Terbium and Rhodamine	as Labels in a Homogene	ous Time-resolved
		Fluorometric Energy Transfer Assay of the β Su	bunit of Human Chorionic	Gonadotropin in Serum,"
		Clinical Chemistry, 45, 855-861 (1999).		
	55	L.L. PEARCE et al., "Role of Metallothionein in	Nitric Oxide Signaling as R	evealed by a Green
		Fluorescent Fusion Protein," Proceedings of the	National Academy of Scie	nces of the United States
		of America, 97, pp. 477-482 (2000).		
	56	M. KORESAWA et al., "Development of a Time-	Resolved Fluorometric De	tection System Using
		Diffusion-Enhanced Energy Transfer," Analytica	l Chemistry, 72, pp. 4904-4	1907 (2000).
	57	T. NAGANO et al., "Specific Detection Method a	and Useful Generating Syst	tem of Singlet Oxygen,"
		Free Radicals in Clinical Medicine, Vol. 7, pp. 3	5-41 (1993).	
	58	I. SAITO et al., "Methyl-Substituted Poly(vinylna	phthalene) as a Reversible	e Singlet Oxygen Carrier,"
		J. Am. Chem. Soc., Vol. 107, pp. 6329-6334, 19	985.	
	59	T. W. Greene et al., "Protective Groups in Orga	nic Synthesis," John Wiley	& Sons, Inc., pp. v-xxi
		and 369-405 (1981).		
	60	J. KABATC et al., "Free Radical Polymerization		Intermolecular Electron
	_	Transfer Process: Kinetic Study 3 ¹ ," Polymer 40	· · · · · · · · · · · · · · · · · · ·	
	61	K. SETSUKINAI et al., "Fluorescence Switching		
		Development of Novel Flourescence Probes to	Detect Reactive Oxygen," .	J. Chem. Soc., Perkin
		Trans. 2, 12, pp. 2453-2457, (2000).	79	India Palala / Adda / Adda / Adda
FXAMINFR		/Taofiq Solola/ DA	TE CONSIDERED /	l aoliq Solola/ 03/31/2008

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

DATE CONSIDERED

P26478.P10			10	519682 - GAU:n1621
FORM PTO-14	49	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. P26478	Application No. 10/519,682
INF		TION DISCLOSURE STATEMENT BY APPLICANT	Applicant Tetsuo NAGANO et al.	
	(Use	e several sheets if necessary)	Filing Date I.A. Filed July 7, 2003	Group 1755
		OTHER DOCUMENTS (Including Author, Title,	Date, Pertinent Pages, Etc.)	
	62	J.W. FIRTH et al., "Some Phenoxy-2H-benzo[b]	pyrans," J. Chem. Research	(S), Vol. 2000, No. 7,
		pp. 308-308 (July 2000).		
(63	J.G. REYES et al., "A Fluorescence Method to I	Determine Picomole Amount	s of Zn(II) in Biological
		Systems," Biol. Res., Vol. 27, pp. 49-56, (1994).		
	64	M. TSUDA et al., "Expression of Zinc Transporte	er Gene, ZnT-1, Is Induced A	After Transient
		Forebrain Ischemia in the Gerbil," The Journal o	f Neuroscience, Vol. 17, No	. 17, pp. 6678-6684
		(September 1, 1997).		
(65	T. KOIKE et al., "A Novel Biomimetic Zinc(II) - F	luorophore, Dansylamidoetl	nyl-Pendant
		Macrocyclic Tetraamine 1,4,7,10-Tetraazacyclo	dodecane (Cyclen)," J. Am.	Chem. Soc., Vol. 118,
		1996, pp. 12696-12703.		
(66	Web site of the Pharmaceutical Society of Japan	n, on February 1, 2003, a co	py of the screenshot is
		enclosed. The subject matter of the screenshot	was then published in an Al	ostract of "The 123 rd
		Annual Congress of the Pharmaceutical Society	of Japan" on March 5, 2003	for presentation No.
		29[P1]I-219 entitled "Development of Fluorescent	nt Probe Having Low Affinity	for Zinc" in the 123 rd
		Annual Congress of the Pharmaceutical Society	of Japan held on March 27-	-29, 2003.
(67	Newport Green: A Catalog of Molecular Probes,	Inc. "Handbook of Fluoresc	ent Probes and
		Research Chemical, Chapter 22 – Section 22.7	Fluorescent Indicators for Z	n ²⁺ and Other Metals",
		6 th Edition by Richard P. Haugland, pp. 531-540	(1996)	
(68	Toshiaki HIRATSUKA, "Tanpakushitsu-Kakusar	n-Kouso (Protein, Nucleic Ad	id and Enzyme)", Vol.
		42, No. 7, pp. 171-176 (1997).		
(69	ANDEREGG et al., Helvetica Chimica Acta, Vo.	. 50, pp. 2330-2333 (1967).	
	70	T. HIRANO et al., "Highly Zinc-Selective Fluores	scent Sensor Molecules Suit	able for Biological
		Applications," Journal of the American Chemica	l Society, Vol. 122, No. 49, p	p. 12399-12400 (2000)
	71	R.P. HAUGLAND, "Handbook of Fluorescent pro	obes and Research Product	s," 9 th Edition
		Supplement, Chapter 20, pp. 805-817 (2002).		
	72	G.K. WALKUP et al., "A New Cell-Permeable FI	uorescent Probe for Zn2+," J	ournal of the American
		Chemical Society, Vol. 122, No. 23, pp. 5644-56	645 (2000).	
	73	J. KAWAKAMI et al., "Ab initio Molecular Orbital	Study of Emission Mechani	ism of 2,6-Bis

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Journal of Computer Chemistry, Japan, Vol. 2, No. 2, pp. 57-62 (2003).

74

EXAMINER

pp 91-103 (1987).

/Taofiq Solola/

DATE CONSIDERED

03/31/2008

(quinolinecarboxy) methylpyridine as Fluorescent Chemosensors for Zinc and Cadmium Ions,"

C.J. FREDERICKSON et al., "A quinoline fluorescence method for visualizing and assaying the histochemically reactive zinc (bouton zinc) in the brain," Journal of Neuroscience Methods, Vol. 20,

P26478.P10				10519682 - GAGhelige
FORM PTO-	1449	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. P26478	Application No. 10/519,682
11		ATION DISCLOSURE STATEMENT BY APPLICANT	Applicant Tetsuo NAGANO et al.	
	(Us	se several sheets if necessary)	Filing Date I.A. Filed July 7, 2003	Group 1755
		OTHER DOCUMENTS (Including Author, Title,	Date, Pertinent Pages, Etc.)	
	75	D. ZALEWSKI et al., "Correlation of apoptosis w	rith change in intracellular	labile Zn(II) using Zinquin
		[(2-methyl-8-p-toluenesulphonamido-6-quinolylo	xy)acetic acid], a new spe	cific fluorescent probe for
		Zn(II)," Biochemical Journal, Vol. 296, Part 2, pp	o. 403-408 (1993).	
-	76	William A. PRYOR et al., "A Practical Method fo	r Preparing Peroxynitrite S	Solutions of Low Ionic
		Strength and Free of Hydrogen Peroxide," Free	Radical Biology & Medicin	e", Vol. 18, No. 1, pp. 75-
		83 (1995).		
	77	Stephen L. HEMPEL et al., "Dihydrofluorescein	Diacetate is Superior for D	etecting Intracellular
		Oxidants: Comparison with 2',7'-Dichlorodihydro	ofluorescein Diacetate, 5(a	nd 6)-Carboxy-2',7'-
±1•		Dichlorodihydrofluorescein Diacetate, and Dihyd	Irorhodamie 123," Free Ra	idical Biology & Medicine,
		Vol. 27, Nos. 1/2, pp. 146-159 (1999).		
	78	Joseph A. HRABIE et al., "New Nitric Oxide-Rel	easing Zwitterions Derived	I from Polyamines," J.
4.212		Org. Chem. Vol. 58, pp. 1472-1476 (1993).		
				V
				
··-·				
<u> </u>				

DATE CONSIDERED 03/31/2008 *EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

/Taofiq Solola/

EXAMINER